5

TUBERCULOSIS AMONG ANIMALS

BY W. A. BREND, M.A., M.B., B.Sc.

[FROM "SCIENCE PROGRESS," NO. 9, JULY 1908]

TUBERCULOSIS AMONG ANIMALS

By W. A. BREND, M.A., M.B., B.Sc.

The splendid work done by the Royal Commission on Human and Bovine Tuberculosis, and the immense mass of observations recorded in the six large volumes of the report and appendix, afford material for research to independent investigators in directions other than those taken by the Committee. One of these is the problem of the curious and marked differences in the degrees of susceptibility to tuberculosis exhibited by the different classes of animals which were the subject of experiment.

The Commission was appointed to determine whether tuberculosis in men and animals is one and the same disease, and if, and under what conditions, transmission of it from animals to men takes place. For the purposes of the inquiry numerous experiments were made on dogs, cats, rabbits, rats, mice, goats, pigs, bovines, monkeys, apes, and guinea-pigs. Some of these animals were found to display remarkable powers of resistance to the disease, others were susceptible to extremely small doses of the virus. But though numerous estimations of the degrees of susceptibility are made and comparisons are drawn, nowhere, in either the report or appendix, is any attempt made to suggest an explanation of these differences. Nevertheless, when all the results scattered through the volumes are collected and compared, an explanation suggests itself which seems to accord fully with all the facts observed.

Let us begin by describing briefly what the results obtained with different classes of animals were.

It will be recalled that two separate and distinct investigations were carried on: one into the effects produced upon animals by the bacillus of bovine tuberculosis, the other into the effects produced by the bacillus of human tuberculosis. In each series experiments were made both by injecting cultures and emulsions of tuberculous lesions, and by feeding the animals upon infected material. Some of the animals so treated died of generalised tuberculosis. Those which survived were killed after the lapse of a certain interval of time, and their organs and tissues were examined for signs of the disease.

In the first series of experiments it was found that rats and mice display the highest powers of resistance. Their capacity for overcoming the disease is enormous. The injection of small or moderate doses of the virus produced no effect at all. Large doses were only sometimes fatal, and even in these cases tuberculous lesions were not found on post-mortem examination, death having resulted from physiological changes brought about by multiplication of the bacilli in all the organs and tissues. Feeding experiments equally demonstrated a high degree of immunity. Twenty-six rats were fed with large quantities of highly infected material for periods of from twelve to twenty-three days, so that they received an enormous dose. On examination, two displayed minute traces of the disease, the rest were unaffected.

Dogs come next in order of power of resistance. They are very little susceptible to the bacillus of bovine tuberculosis either by subcutaneous inoculation or by feeding. They are more susceptible to intraperitoneal inoculation.

In cats the results of feeding were very similar to those obtained with dogs. They displayed, however, a smaller power of resistance to the effects of inoculation. Kittens were more susceptible than cats.

Next comes a group consisting of goats, calves, and pigs, between which no very great differences in the degrees of susceptibility can be observed, all being readily infected by moderate doses of the virus either by inoculation or by feeding. Frequently, however, the disease was not fatal. Calves were slightly less susceptible than goats, and goats less susceptible than pigs.

At the end of the scale come rabbits, monkeys, anthropoid apes, and guinea-pigs. All these are extraordinarily sensitive to the action of the bacilli. In the case of rabbits an attempt to determine the minimum fatal dose of a culture showed that so small an amount as one ten-millionth of a milligramme produced generalised tuberculosis. A chimpanzee succumbed to ·001 milligramme when injected subcutaneously, and two others to ·01 milligramme when given with food. The sensitiveness of guinea-pigs is so marked that inoculation of them by a suspected material may be used as a test for the presence of the bacilli when the latter are too few in number to be detected by microscopic examination.

In the second series of experiments—those made with tubercle bacilli of human origin—the viruses employed were divided into two groups, those of Group I. being much more virulent than those of Group II. The same species of animals were used, and the results obtained were very similar to those observed with bovine material. Rats and mice again displayed high powers of resistance. Infection did not cause visible tuberculous lesions; but after the introduction of large doses, multiplication of the bacilli took place, and death resulted from a condition which has been called "tuberculous septicæmia."

Dogs showed only slight traces of the disease when inoculated or fed with the bacilli of Group II. The single experiment made with Group I. caused death from general tuberculosis.

The few observations made upon cats showed that the species was highly resistant to the bacilli of Group II., but was more susceptible to those of Group I.

The goat, pig, ox, and rabbit were highly susceptible to the viruses belonging to Group I., but in most cases only showed slight disease after infection by Group II. Rabbits, however, were less resistant than calves, and with some viruses of Group II. showed progressive generalised tuberculosis.

Chimpanzees, monkeys, and guinea-pigs were readily infected by the bacilli of either group, and this in very small doses.

Combining the results from these two sets of experiments, and sinking small differences, we find that the order into which the various classes of animals fall when arranged according to their degrees of susceptibility to tuberculosis is as follows:

Rats and Mice.
Dogs.
Cats.
Pigs, Goats, Bovines.
Rabbits.
Guinea-pigs, Monkeys, Apes.

What explanations can be suggested to account for the enormous differences between the first and last of this series? In the first place, it seems clear that the degree of resistance cannot be a function of the natural order; for we find at one end of the scale animals so dissimilar as rats and dogs resembling each other in their high degree of immunity, and, at the other end, guinea-pigs and chimpanzees alike exhibiting marked susceptibility. On the other hand, animals belonging to the same natural order—rodentia—occupy positions at the extreme ends of the scale. The Commissioners themselves do not appear to have recognised fully the complete absence of relationship between natural order and degree of susceptibility, for they remark on p. 14 of the report "the fact that the bacillus of bovine tuberculosis can readily by feeding as well as by subcutaneous injection give rise to generalised tuberculosis in the anthropoid ape, so nearly related to man, . . . has an importance so obvious that it need not be dwelt upon." Yet the experiments clearly establish that natural order has no significance whatever in this connection.

More importance might be attached to the question of diet, for carnivorous animals appear to have distinctly greater powers of resistance than herbivorous.

Dr. Archdall Reid has, however, furnished us with an explanation of the different degrees of susceptibility to tuberculosis exhibited by different branches of the human family, which, when extended to animals, will be found to agree in a remarkable manner with the facts. He has investigated the prevalence of zymotic diseases among a large number of races both of the Old and New Worlds, and has shown conclusively that a community exhibits a resistance to a disease which is in strict proportion to its past experience of it. The European peoples have suffered from tuberculosis at least since the days of Hippocrates, and they have now, in spite of the high death-rate which they still show, acquired a degree of immunity which can only be measured by observing the effects of the disease upon virgin soil. The history of the peoples of the New World furnishes an opportunity. Tuberculosis was carried thither in the sixteenth century, and among an unprotected native populace its effects were tragic. Whole tribes disappeared before it. The Caribbean and Tasmanian are gone. The Red Man only lingers on in spots artificially isolated from the contact of civilisation.

Such a relationship between experience and disease is fully in accord with the theory of evolution by natural selection.

A zymotic disease which persists from generation to generation and is not merely of occasional occurrence, eliminates in each generation those individuals who are most susceptible to it, or who are unable to develop adequate powers of resistance when attacked. Hence a progressively increasing degree of immunity and a continuously falling death-rate. Many other instances of this phenomenon have been investigated by Dr. Archdall Reid. Malaria is deadly to Europeans, but comparatively innocuous to West African natives who have undergone evolution against it; measles causes a high mortality among the Polynesians; Esquimaux die from vaccination, while Europeans usually recover from small-pox. Alcoholism, which he regards as governed by the same influences, is least among the ancient peoples round the Mediterranean who have had alcohol longest; greater among northern Europeans; and rampant among the primitive peoples of Australia and America to whom the poison is new.

If, with these facts in mind, we now look again at the list of animals arrived at above, we see at once that it corresponds exactly with that of the degree of closeness of their association with man, *i.e.* with the opportunities they have had in the past of acquiring tuberculosis from him. Rats and mice, which come first, though not ordinarily regarded as domesticated, are nevertheless very highly so from the scientific point of view. They are constantly and intimately associated with man. They inhabit his cellars and his sewers; they feed upon his refuse and the infected sweepings of his streets and pavements, which he persists in regarding as the appropriate place for expectoration. In such a habitat they must have undergone stringent natural selection against tuberculosis, the effects of which are seen in the extraordinary degree of immunity they now possess.

Dogs and cats come next. These animals have for long been closely associated with man, but not under such adverse conditions as rats. They inhabit the better ventilated parts of his dwellings, and are cleaner feeders. They are following the same path as the rats, but have not yet developed the high powers of resistance possessed by the latter. The greater susceptibility shown by the cat as compared with the dog is probably to be explained by their past histories. It is not possible to say positively which has been domesticated the longer, for though the bones of both have been found associated with the remains of prehistoric man, this may merely indicate that they were used for food, and representations of both animals are found upon the ancient Egyptian monuments. Yet there can be little doubt that the cat is nearer the original wild form than the dog. This is shown by its instincts and habits. The cat, for instance, never exhibits the same devotion to men that the dog does; and, as Darwin points out, cats are always eager to attack poultry, while dogs, even when quite young, rarely show such a tendency. Further, the nocturnal habits of the domesticated cat, and the survival of the wild cat, enabled frequent crossings to occur long after such a process became rare or impossible for dogs.

Next comes a group comprising some of our familiar domesticated cattle, viz. goats, pigs, cows, and calves. These animals are only at times under adverse conditions. Whilst in the fields they enjoy their natural environment. But when they are shut up in stalls and byres they breathe a confined and tainted atmosphere, they are brought in contact with man, they risk catching his diseases. Under such circumstances the struggle has been only moderately severe, and the susceptibility of these animals to tuberculosis accordingly remains considerable.

At the end of the list are rabbits, monkeys, apes, and guinea-pigs, all wild forms, for the last, though now bred in captivity, was not introduced into Europe from South America until the sixteenth century. In their native forests and prairies these animals have never felt the touch of civilisation. They have never been subjected to any selection against tuberculosis, and, consequently, in their totally unprotected state, the disease attacks them with terrible virulence.

One point more may be mentioned. When both adult and young forms of the same species were examined, it was invariably found that the latter displayed greater susceptibility than the former. Thus calves were more susceptible than cows, kittens than cats, and puppies than dogs. This again agrees with what is found in the human species, for, with the exception of pulmonary tuberculosis, all forms of the disease are of much greater prevalence among children than among adults; and as regards such affections as measles and scarlet fever, their enormously greater prevalence among the young has led to their being spoken of as "children's diseases." This lends further support to the theory of the gradual acquirement of immunity by natural selection, for, as Dr. Archdall Reid points out, "children represent a stage in the life history of the race when the general evolution against disease was not so advanced."

The gradual increase of immunity in the series of animals described above seems to afford a striking instance of progressive adaptation. It would be interesting, and would serve as some test of the theory, to know how far the relationship holds among animals other than those examined by the Committee. We should, for example, expect horses and sheep to resemble generally bovines and pigs; while deer, foxes, and squirrels should, like rabbits, be highly susceptible. Of particular interest would be some experiments on voles and other forms nearly allied to rats, but living in a different environment.

It is difficult to regard the variation upon which natural selection has acted in bringing about this evolution as other than "continuous." The observation, therefore, has additional value at a time when adherents of the advanced Mendelian school are suggesting that discontinuous variations have alone played a part in causing evolutionary changes. From the practical point of view the lesson taught is that while we may endeavour to maintain the health of our domesticated cattle by surrounding them with sanitary conditions, every effort should be made to discourage breeding from tainted individuals. It is only by assisting nature that we shall ever be able to call into existence naturally resistant stocks.